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## Preoperative sarcopenia is a predictor of postoperative pulmonary complications in esophageal cancer following esophagectomy: A retrospective cohort study

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### ABSTRACT

**Objectives:** The number of geriatric patients with esophageal cancer has been increasing. Geriatric syndromes such as sarcopenia might adversely affect postoperative recovery. The aim of this study was to evaluate the relationships between sarcopenia and postoperative complications, and the associations between sarcopenia and perioperative functional changes in patients with esophageal cancer following esophagectomy.

**Materials and methods:** Participants comprised 104 patients who underwent esophagectomy from July 2011 to April 2015. Preoperative sarcopenia was diagnosed by the presence of low muscle mass and low physical functions according to Asian Working Group for Sarcopenia criteria. Low physical function was defined by loss of grip strength and/or slow walking speed. Postoperative pulmonary, cardiac, infectious, and surgical complications were extracted. Perioperative functional changes were calculated (value at postoperative day 30 – value before surgery). For statistical analyses, both uni- and multivariate logistic regression analyses were performed.

**Results:** Twenty-nine patients (27.9%) were diagnosed with sarcopenia. The incidence of postoperative pulmonary complications was significantly higher in the sarcopenia group (37.9%) than in the non-sarcopenia group (17.3%;  $P = 0.04$ ). There was no relationship between sarcopenia and other complications or perioperative functional changes. Multivariate analysis identified sarcopenia (odds ratio (OR), 3.13; 95% confidence interval (CI), 1.12–8.93) and high Brinkman index (OR, 3.46; 95% CI, 1.20–11.77) as independent risk factors for the development of pulmonary complications.

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**Conclusion:** The assessment of sarcopenia may be useful to predict the postoperative pulmonary complications following esophagectomy. On the other hand, sarcopenia does not predict cardiac, infectious, and surgical complications or perioperative function.

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## 1. Introduction

Esophageal cancer is a highly aggressive malignant tumor, and esophagectomy is associated with high morbidity and mortality rates.<sup>1,2</sup> The proportion of older patients with esophageal cancer has been increasing in the United States, Europe, and Japan.<sup>3-5</sup> The impact of geriatric syndrome on esophagectomy is of considerable importance.

Sarcopenia, characterized by progressive generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, loss of independence, and death<sup>6,7</sup> is a common geriatric syndrome. The European Working Group on Sarcopenia in Older People recommends using the presence of both low muscle mass and low muscle function to diagnose sarcopenia.<sup>8</sup> In the previous studies, sarcopenia has been identified as an independent predictor of postoperative pulmonary complications following esophagectomy,<sup>9,10</sup> but the diagnosis of sarcopenia in those studies was made based on the presence of low muscle mass alone. Furthermore, no published reports have described the effects of preoperative sarcopenia on perioperative functional change. We hypothesized that sarcopenia defined by both low muscle mass and low muscle function predicted postoperative complications and perioperative functional changes in patients with esophageal cancer following esophagectomy.

The aim of this study was to assess preoperative sarcopenia using both muscle mass and function and to evaluate the relationship between sarcopenia and postoperative outcomes such as postoperative complications and perioperative functional change in patients with esophageal cancer who underwent esophagectomy.

## 2. Materials and Methods

### 2.1. Participants

The present study was a retrospective cohort study. This study was conducted between July 2011 and April 2015 at the single university hospital located in the urban area. Patients with esophageal cancer were eligible if they were scheduled to undergo definitive esophagectomy. Patients were excluded if they had a recurrent cancer or declined to consent. The study was approved by the ethics committee of Kobe University Graduate School Health Science (approval number 112) and registered with the University Hospital Medical Information Network. This study was performed in accordance with the ethical standards established in the 1964 Declaration of Helsinki and later amendments.

### 2.2. Measurements

Preoperative laboratory data and treatment information were collected from the medical records of patients. Laboratory data

included predicted vital capacity (VC), forced expiratory volume in 1 s (FEV1.0) as a percentage of forced VC, C-reactive protein (CRP), and serum albumin. Treatment information was as follows: preoperative clinical stage, comorbidity, smoking history, performance status, weight loss over the past 6 months, preoperative treatment, operative time, blood loss, duration of inhibited oral intake, and duration of hospitalization after surgery. Clinical staging was based on the TNM classification (6th edition)<sup>11</sup> defined by the Union for International Cancer Control. Smoking history was assessed using the Brinkman index defined as numbers of cigarette smoked per day times smoking years. Performance status was defined based on the Eastern Cooperative Oncology Group Performance Status. Neoadjuvant chemotherapy with cisplatin plus 5-fluorouracil was provided as preoperative treatment. We calculated the Geriatric Nutritional Risk Index (GNRI)<sup>12</sup> using preoperative serum albumin and body weight.

Body composition, muscle strength, mobility, fatigue, and health-related quality of life (HRQoL) were assessed before esophagectomy and on postoperative day (POD) 30. We prepared the assessment manual to reduce potential measurement bias. Body composition was assessed using multi-frequency bioelectrical impedance with eight electrodes (DF-860; Yamato, Hyogo, Japan). With this method, body weight, lean body mass, and skeletal muscle mass were measured. Grip strength was measured using a handheld dynamometer (GRIP-D; Takei Ltd., Niigata, Japan) in accordance with the reliable methods reported previously.<sup>13</sup> Mobility was measured using the Short Physical Performance Battery (SPPB),<sup>14</sup> assessing standing balance, walking speed, and ability to rise from a chair (total score, 0–12; higher score suggesting better mobility). Fatigue and HRQoL were measured using the Functional Assessment of Chronic Illness Therapy: Fatigue (FACIT-F)<sup>15</sup> and the Functional Assessment of Cancer Therapy—General (FACT-G),<sup>16</sup> respectively. The FACT-G total score for the Physical, Social/Family, Emotional, and Functional subscales was used. Higher scores on the FACIT-F and FACT-G represent less fatigue and better quality of life, respectively.

### 2.3. Definition of Sarcopenia

Sarcopenia was defined as low muscle mass plus low muscle strength and/or low physical performance according to the Asian consensus definition.<sup>17</sup> Low muscle mass was defined by appendicular skeletal muscle mass divided by squared height of  $<7.0 \text{ kg/m}^2$  for men and  $<5.7 \text{ kg/m}^2$  for women. Low muscle strength was defined by handgrip strength of  $<26 \text{ kg}$  for men and  $<18 \text{ kg}$  for women. Low physical performance was defined by gait speed of  $<0.8 \text{ m/s}$ . In the non-sarcopenia group, patients with low muscle mass were described as showing presarcopenia. In the sarcopenia group, patients were described as showing severe sarcopenia when all three criteria were met.

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